Erdheim-Chester disease

Erdheim-Chester disease is a rare disorder characterized by histiocytosis, a condition in which the immune system produces excess quantities of cells called histiocytes. Histiocytes normally function to destroy foreign substances and protect the body from infection. Erdheim-Chester disease is classified as a form of non-Langerhans cell histiocytosis to distinguish it from Langerhans cell histiocytosis, which involves accumulation of a specific type of histiocyte called Langerhans cells. In Erdheim-Chester disease, histiocytosis leads to inflammation that can damage organs and tissues throughout the body, causing them to become thickened, dense, and scarred (fibrotic); this tissue damage may lead to organ failure.

People with Erdheim-Chester disease often have bone pain, especially in the lower legs and upper arms, due to an abnormal increase in bone density (osteosclerosis). Damage to the pituitary gland (a structure at the base of the brain that produces several hormones, including a hormone that controls the amount of water released in the urine) may result in hormonal problems such as a condition called diabetes insipidus that leads to excessive urination. Abnormally high pressure of the cerebrospinal fluid within the skull (intracranial hypertension) caused by accumulation of histiocytes in the brain may result in headaches, seizures, cognitive impairment, or problems with movement or sensation. People with this condition can also have shortness of breath, heart or kidney disease, protruding eyes (exophthalmos), skin growths, or inability to conceive a child (infertility). Affected individuals may also experience fever, night sweats, fatigue, weakness, and weight loss.

The signs and symptoms of Erdheim-Chester disease usually appear between the ages of 40 and 60, although the disorder can occur at any age. The severity of the condition varies widely; some affected individuals have few or no associated health problems, while others have severe complications that can be life-threatening.

Frequency

Erdheim-Chester disease is a rare disorder; its exact prevalence is unknown. More than 500 affected individuals worldwide have been described in the medical literature. For unknown reasons, men are slightly more likely to develop the disease, accounting for about 60 percent of cases.

Genetic Changes

More than half of people with Erdheim-Chester disease have a specific mutation in the *BRAF* gene. Mutations in other genes are also thought to be involved in this disorder.

The *BRAF* gene provides instructions for making a protein that helps transmit chemical signals from outside the cell to the cell's nucleus. This protein is part of a signaling pathway known as the RAS/MAPK pathway, which controls several important cell functions. Specifically, the RAS/MAPK pathway regulates the growth and division (proliferation) of cells, the process by which cells mature to carry out specific functions (differentiation), cell movement (migration), and the self-destruction of cells (apoptosis).

The *BRAF* gene mutation that causes Erdheim-Chester disease is somatic, which means that it occurs during a person's lifetime and is present only in certain cells. The mutation occurs in histiocytes or in immature precursor cells that will develop into histiocytes. This mutation leads to production of a BRAF protein that is abnormally active, which disrupts regulation of cell growth and division. The unregulated overproduction of histiocytes results in their accumulation in the body's tissues and organs, leading to the signs and symptoms of Erdheim-Chester disease.

The *BRAF* gene belongs to a class of genes known as oncogenes. When mutated, oncogenes have the potential to cause normal cells to become cancerous. Researchers disagree on whether Erdheim-Chester disease should be considered a form of cancer because of the unregulated accumulation of histiocytes.

Inheritance Pattern

This condition is not inherited. It arises from a somatic mutation in histiocytes or their precursor cells during an individual's lifetime.

Other Names for This Condition

- lipid granulomatosis
- polyostotic sclerosing histiocytosis

Diagnosis & Management

Other Diagnosis and Management Resources

- Histiocytosis Association: Erdheim-Chester Disease Diagnosis and Treatment
  https://www.histio.org/page.aspx?pid=405

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html

- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Bone Pain or Tenderness
  https://medlineplus.gov/ency/article/003180.htm
- Encyclopedia: Diabetes Insipidus
  https://medlineplus.gov/ency/article/000377.htm
- Encyclopedia: Histiocyte
  https://medlineplus.gov/ency/article/002374.htm
- Encyclopedia: Histiocytosis
  https://medlineplus.gov/ency/article/000068.htm
- Health Topic: Diabetes Insipidus
  https://medlineplus.gov/diabetesinsipidus.html
- Health Topic: Immune System and Disorders
  https://medlineplus.gov/immunesystemanddisorders.html

Genetic and Rare Diseases Information Center

- Erdheim-Chester disease
  https://rarediseases.info.nih.gov/diseases/6369/erdheim-chester-disease

Educational Resources

- Disease InfoSearch: Erdheim-Chester Disease (ECD)
  http://www.diseaseinfosearch.org/Erdheim-Chester+Disease+(ECD)/2628
- MalaCards: erdheim-chester disease
  http://www.malacards.org/card/erdheim_chester_disease
- Orphanet: Erdheim-Chester disease
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=35687

Patient Support and Advocacy Resources

- ECD Global Alliance
  http://erdheim-chester.org/
- Histiocytosis Association
  https://www.histio.org/page.aspx?pid=403#.VTFTCZOauSi
- Intracranial Hypertension Research Foundation
  http://ihrfoundation.org/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Erdheim-Chester+disease%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Erdheim-Chester+Disease%5BMAJR%5D%29+AND+%28Erdheim-Chester+disease%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

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